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| 10/517,898 | 07/27/2005 | Warren Strober | 14014.0410U1 | 5707 |

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| EXAMINER | |
|---|---|
| OUSPENSKI, ILIA I | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/517,898 | STROBER ET AL. | |
| | Examiner | Art Unit | |
| | ILIA OUSPENSKI | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *38-84* is/are pending in the application.

4a) Of the above claim(s) *49-51,62-64,72 and 74-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-48,52-61,65-71 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/04;10/17/05;7/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's remarks filed on 10/14/2008 are acknowledged.

Claims 38 – 84 are pending.

2. Applicant's election with traverse of Group IV (claims 38 – 48, 52 – 61, 65 – 71, and 73, drawn to a method of treating or preventing an inflammatory response of colitis by administering an antibody that binds to IL-13) in the reply filed on 10/14/2008 is acknowledged.

The traversal is on the grounds that allegedly the prior art reference of US Patent No. 6,696,545, cited in the Restriction Requirement as anticipating the special technical feature of the present inventions that defines the contribution over the prior art, does not explicitly teach a method of treating an inflammatory response in colitis using a substance that inhibits production of IL-13. Specifically, Applicant asserts that the reference teaches a list of inflammatory cytokines, including IL-13, and a list of inflammatory responses, including colitis, and further relies on knowledge in the art to select specific cytokines for treatment of appropriate inflammatory responses.

This is not found persuasive because, contrary to Applicant's assertion, there appears to be no indication in the teachings of the reference that would invite the skilled artisan to search for cytokines appropriate for treating specific diseases. For example, the following passage (column 3 lines 54 – 63) is showed that the inventors of the '545 Patent contemplated using an inhibitor of every one of the listed cytokines for treatment of every one of the listed conditions, and therefore each combination of an inhibitor and condition is explicitly taught by the reference:

"The peptides described herein also find use for inhibiting the production of inflammatory cytokines (e.g., interferon-.gamma., IL-1, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IL-16, MIP1.alpha., etc.), thereby being useful for inhibiting inflammatory responses associated with various disorders such as rheumatoid arthritis, septic shock, Crohn's disease, colitis, allergic reactions, autoimmune diseases, and the like, for inhibiting the activity of heme-based enzymes such as heme oxygenase, nitric oxide synthase, etc., and delaying the onset of IDDM in a patient at risk for developing IDDM, both in vitro and in vivo."

Applicant further argues that the restriction requirement does not provide sufficient basis to indicate that examination of more than one invention would overly burden the Examiner.

In response, search burden is not a consideration in applications filed under 35 USC 371.

Therefore, the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 49 – 51, 62 – 64, 72, and 74 – 84 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

***Claims 38 – 48, 52 – 61, 65 – 71 and 73 are presently under consideration.***

3. The following is a quotation of the **second paragraph of 35 U.S.C. 112**.

*The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

4. Claims 47 and 60 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47 and 60 are indefinite in the recitation "wherein the antibody prevents antigen recognition," because it is unclear which antigen is being recognized and by what substance. Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

5. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

6. Claims 38 – 48, 52 – 61, 65 – 71 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the claimed method, because Applicant is not in possession of the generically recited "substance that modulates NK-T cell activity," including a generically recited antibody of undefined specificity (claims 46 – 48); or a generically recited "substance that modulates IL-13 activity," including a generically recited antibody of undefined specificity (claims 59 – 60 and 71).

The instant specification discloses at page 4, lines 14 – 20, non-limiting examples of several antibodies and polypeptides which are characterized as "substances of the present invention." However, the breadth of the generic recitations in the instant claims encompass substances of any chemical nature or structure, limited only by their ability to modulate NK-T cell activity or IL-13 activity. In the absence of a disclosure in the instant specification of sufficiently detailed, relevant identifying characteristics, such as complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics, the skilled artisan cannot envision all the contemplated "substances" encompassed by the instant claims.

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, §1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol.

66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

7. Claims 38 – 44, 46 – 48, 52 – 61, 65 – 68, 70, 71 and 73 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The specification does not enable one of skill in the art to "prevent" an inflammatory response of colitis, except for oxazolone colitis, without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of

experimentation required to enable one of skill in the art to practice the claimed invention.

The instant specification discloses at page 27 a working example wherein neutralization of IL-13 is effective in reversing the symptoms of inflammation in the oxazolone-induced colitis in mice (lines 21 – 35). Kawada et al. (World J. Gastroenterol., 2007, 14: 5581 – 5593), in reviewing available animal models of human inflammatory bowel disease, conclude that oxazolone-induced mouse model shares some aspects of human pathology and is suitable, along with other models, for evaluating prospective treatments (see entire document, in particular e.g. page 5581 – 5583 and page 5588).

However, the burden of enabling the prevention of a disease is greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. The specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to colitis, which is required to achieve “prevention” of the disease as presently claimed. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed methods in preventing the disease. Accordingly, undue experimentation is necessary to determine screening and testing protocols to practice the presently claimed methods as they relate to prevention of inflammatory response of colitis in a subject.

8. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

9. Claims 38 – 45, 52 – 58, and 65 – 70 are rejected under **35 U.S.C. 102(e)** as being anticipated by Buelow et al. (US Patent No. 6,696,545; of record; see entire document).

The teachings of Buelow et al. have been discussed in section 2 supra, and include peptides which inhibit production of IL-13 and can be used for treatment of inflammatory responses associated with colitis (e.g. column 3 lines 54 – 63). Substances that inhibit IL-13 production inherently modulate NK-T activity, regardless of whether or not this property was known at the time the invention was made.

Therefore, the teachings of the reference anticipate the instant claimed invention.

10. Claims 38 – 48, 52 – 61, 65 – 71 and 73 are rejected under **35 U.S.C. 102(e)** as being anticipated by Heavner et al. (US Pat. Pub. No. 2004/0023337; see entire document).

Heavner et al. teach antibodies to mutant forms of IL-13 (e.g. paragraphs 0003 and 0014), and further teaches that these can be used for treatment of diseases, such

as inflammatory bowel disease, ulcerative colitis and Crohn's disease (e.g. paragraph 0176). Antibodies to IL-13 inherently modulate NK-T activity, regardless of whether or not this property was known at the time the invention was made.

Therefore, the teachings of the reference anticipate the instant claimed invention.

11. Claims 38 – 45, 52 – 58, and 65 – 70 are rejected under **35 U.S.C. 102(e)** as being anticipated by Cohen et al. (US Pat. Pub. No. 2004/0022787; see entire document) as evidenced by Heller et al. (Immunity, 2002, 17: 629 – 638; see entire document).

Cohen et al. teach the use of CTLA4Ig fusion protein for treatment of Crohn's disease and ulcerative colitis (e.g. paragraph 0275).

One of skill in the art is aware that CTLA4Ig inhibits activation of CD28 by B7-1 and B7-2 molecules in the course of both normal and pathological immune response.

Heller et al. provide evidence that activation via CD28 is required for NK-T activation and IL-13 production (e.g. pages 629 – 630, bridging paragraph).

One of skill in the art would therefore understand that CTLA4Ig is a substance that modulates NK-T cell activity and IL-13 activity, and as such, the teachings of Cohen et al. anticipate the instant claimed invention.

***12. Conclusion: no claim is allowed.***

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is (571)272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ILIA OUSPENSKI/
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Art Unit 1644

January 3, 2009